October 25, 1999

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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, Maryland 20852

Re: Docket No. 99D-2635; Draft Guidance for Industry on ANDA's: Blend Uniformity Analysis
Federal Register, Friday, August 27, 1999 (64 FR 46917)

Dear Sir or Madame:

Geneva Pharmaceuticals, Inc. appreciates the opportunity to respond to the FDA's draft guidance, *ANDAs: Blend Uniformity Analysis*. At this time, Geneva Pharmaceuticals, Inc. urges the FDA to **NOT** implement the draft guidance in its current form.

Major concerns with this draft guidance are as follows:

- According to 21 CFR 211.110 (a) and Judge Wolin's statement in U.S. *v.* Barr, Blend Uniformity Analysis (BUA) is required for development and validation stages and correlated to a blend time which is monitored on all future batches. In these documents, it is **NOT** stated or inferred that BUA is required for commercial batches after validation.

- The proposed acceptance criteria does **NOT** match the definition in 21 CFR 211.110. It is defined, therein, that valid in-process specifications shall be consistent with drug product final specifications and that the specification shall be derived from process average and variability data. The proposed specification is not consistent with USP specifications for content uniformity, including the disallowance of a two-tiered acceptance criteria, and allows for no variability due to sampling bias.

Minor concerns with this draft guidance are as follows:

II. SCOPE

- Paragraph 1: Second sentence does not match the USP definition.
- Paragraph 2 : Clarify dosage forms which require USP content uniformity analysis by referring to footnote 4 and eliminating the bullet points.
- Paragraph 3: Clarify filing requirements to remove a BUA test from an approved ANDA in cases where the test is exempt for a product, according to the USP definition. Include filing requirements for removing a BUA test from an approved ANDA after validation.

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III. SAMPLING SIZE AND PROCEDURES

- Paragraph 2: The first sentence should state "Samples for BUA are collected from intermediate containers."
- Paragraph 2: The second sentence should state "For more than one intermediate container, an appropriate sampling plan should be devised for BUA of bioequivalence and/or test batches.
- Paragraph 3: The second sentence should just state "Since the purpose of BUA is to assess uniformity and homogeneity of a blend, composite sampling is not appropriate."
- Paragraph 3: The third sentence, "The weight of the sample tested should be equivalent to the dosage used," should be moved to paragraph one and incorporated into the first sentence as follows: "The recommended sample weight of the blend material tested should be equivalent to the dosage used, but is no more than three times the weight of an individual dose."
- Paragraph 4: Clarify definition of common blend versus an intermediate, which may have its own release testing criteria in an approved ANDA.

Attachments A and B

- Need clear definition of simple dosage forms, complex dosage forms, and complex processes.

Glossary

- The definitions are not necessary in this document.

Footnotes

- Footnote 3: Comment. It is recommended that any BUA requirements be equally applicable to ANDAs and NDAs.

In conclusion, Geneva Pharmaceuticals, Inc. urges the FDA to cease implementation of this draft guidance in its current form. Geneva Pharmaceuticals, Inc. joins the Generic Pharmaceutical Industry Association (GPIA) and the Parental Drug Association (PDA) in urging the FDA to participate in a joint Industry-FDA workshop in which all parties can come to a common position.

Sincerely,

David L. McAleese

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SUBJECT:

Docket No. 99D-2635; Draft Guidance for Industry on ANDA's: Blend Uniformity Analysis

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